REMARKS

Claims 1-25 and 27-29 are pending in the application. The Office Action indicated that rejection of claims under 35 U.S.C. §§ 102(b), 102(e)/(f), and 103(a) were withdrawn. Claims 1-25 and 27-29 are rejected under 35 U.S.C. 112 on various grounds as summarized below.

Applicants' representative Dr. Rex M. Bitner of Promega Corporation, to which the instant invention is assigned, and the undersigned attorney met with Examiner Sisson on March 11, 2004 to discuss placing the application in condition for allowance. The time and courtesies extended to Dr. Bitner and the undersigned are acknowledged with appreciation. In accordance with the rules, this document will confirm the substance of that interview.

Specifically, the objection to the specification and rejections under 35 U.S.C. 112, first and second paragraphs were discussed. Examiner Sisson indicated that amendments to the claims to include a limitation to methods employing magnetic particles having a particle size of about 1 to 15 μm would be favorably considered, as would amendments to clarify that certain of the methods permit separation of classes of nucleic acids. In addition, Examiner Sisson suggested deleting the term "directly" to describe adsorption of nucleic acid to the particles.

In view of the amendments above and the arguments below, Applicants respectfully request reconsideration on the merits of the application, withdrawal of the objection and rejections, and allowance of all pending claims.

Amendments to the claims

Claims 1, 7, 8, 15, 16, 19, and 21 are currently amended. Claims 1, 7, 8, 15, 16, 19, and 21 were amended to include a limitation to particles having a particle size of about 1 to 15 μm. Support for the amendment can be found in the specification (e.g., please see page 12, lines 11-22). Claims 1, 8, 15, 16, 19, and 21 were amended to delete the term "directly" modifying adsorbs. Support for the amendment is found, for example, in the claims as originally filed. Claims 19 and 21 were amended to clarify that the target nucleic acid is selected from the group consisting of plasmid DNA, total RNA, mRNA, and genomic DNA. Support for the amendment can be found, for example, at page 1, lines 20-24.

Objection to the specification

The Office Action objects to the specification because the Examiner asserts that the specification does not identify with particularity where the material is found in the cited document. The Office Action concludes that the document cannot be relied upon to satisfy the written description and enablement requirements. The incorporation is reproduced below:

> "Such preferred ion exchange ligands and pH dependent ion exchange matrices which incorporate such ligands are described in U.S. Patent Application Ser. No. 09/312,172, now U.S. Patent No. 6,310,199, for an invention titled pH DEPENDENT ION EXCHANGE MATRIX AND METHOD OF USE IN THE ISOLATION OF NUCLEIC ACIDS, incorporated by reference herein, an application filed concurrently with the provisional patent application on which the present non-provisional patent application is based."

Although Applicants incorporated the entire '199 Patent by reference, Applicants refer specifically to "ion exchange ligands and pH dependent ion exchange matrices which incorporate such ligands." With all due respect, it is well within the ability of one skilled in the art to identify that material within the '199 Patent that relates to pH dependent ion exchange particles. Specifically, one skilled in the art would appreciate that Applicants were intending to refer to Examples 3, 5, or 7 of the '199 Patent. Furthermore, the specification of the instant application itself describes the preparation of pH dependent ion exchange particles (e.g., see Example 3).

The entire '199 Patent was incorporated by reference simply to reduce the volume of this applciation. Incorporation of the patent was not necessary to describe the claimed invention or to provide an enabling disclosure. Those requirements were met by the specification of the instant application as originally filed. In view of the foregoing, Applicants respectfully request withdrawal of the objection.

Rejections under 35 U.S.C. 112, first paragraph, written description

Claims 1-25 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement for failure to recite a limitation as to particle size. The Examiner acknowledged in the Office Action that particles having a particle size of

about 1 to 15 μm are supported by the specification, and indicated that claims drawn to methods using particles having a size of about 1 to 15 μm would be favorably considered.

Applicants respectfully traverse the rejection, and expressly reserve their right to pursue broader claims in a continuation application. However, in order to advance prosecution, Applicants have amended independent claims 1, 7, 8, 15, 16, 19, and 21 to recite particles having a particle size of about 1 to 15 μm, as defined in the specification at page 12, lines 16-22. One of skill in this art will appreciate that the emphasis in the amendment to claims 1, 7, 8, 15, 19, and 21 should be understood to be on the word "about." Particles having a diameter above the upper limit or below the lower limit are most certainly within the contemplation of the claim coverage. The fact of the non-rigid nature of the diameter is emphasized at page 12 where a diameter variation (±10 μm) is discussed.

Applicants submit that the amendment overcomes the written description rejection of claims 1, 7, 8, 15, 16, 19, and 21, as well as claims dependent claims 2-6, 9-14, 17, 18, 20, and 22-25, which depend directly or indirectly from claims 1, 8, 16, or 21. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. first paragraph for failing to satisfy the written description requirement be withdrawn.

Rejections under 35 U.S.C. 112, first paragraph, enablement

The November 13, 2003 Office Action indicates at paragraph 6 that claims 1-25 and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The bases for the rejections are summarized below.

A. Claims 1-7

Paragraphs 7-11 of the Office Action address the rejection of claims 1-7. Claims 1-7, as amended, are drawn to methods of using pH dependent ion exchange magnetic particles or silica magnetic particles to concentrate or harvest cells, comprising, in part, combining cells with magnetic particles having a particle size of about 1 to 15 μm, under conditions wherein the cells selectively adsorb to the particles thereby forming a complex.

Based on its conclusion that the incorporation of the '199 Patent was not proper, the Office Action asserts that claims 1-7 are not enabled. The Office Action identified Example 8 as being the most relevant to the claims, which the Office Action characterizes as teaching that "multiple and separate aliquots of Mag-IE-glycidyl-histidine particles were used to first bind unidentified "cells" and that subsequent to lysis, Mag-IE-glycidyl-histidine particles were used to bind the nucleic acid. The Office Action asserts that the specification does not

teach that the second aliquot was in the form of magnetic particles, and that the specification does not teach what type of cell was used.

Applicants direct the Examiner's attention to the fact that Example 8 includes three separate parts. The part that is relevant to claims 1, 2, 6, and 7 is part A, which relates to concentrating bacterial cells. The cell type employed in this Example, identified on page 26, line 25, is DH5α/pGem3Zf+. As one of skill in the art would appreciate, and as is explained in Example 6, DH5α is a line of *Eschericia coli* that is commonly used in cloning. It is well known in the art, as one skilled in the art would appreciate, that DH5α/pGem3Zf+ refers to *Eschericia coli* DH5α containing a pGEM vector that includes the origin of replication of the filamentous phage f1.

In addition to Example 8, which describes isolation of bacterial cells, Example 10 describes concentration of white blood cells from whole blood. This Example clearly provides support for claims 1 and 3-7.

Applicants note that although one may subsequently isolate nucleic acids from cells concentrated according to claims 1-7, there is no requirement that nucleic acids be isolated from the cells.

B. Claims 21-25 and 27-29

The rejection of claims 21-25 and 27-29 under 35 U.S.C. 112, first paragraph as not being enabled is addressed in paragraphs 12-16 of the Office Action.

At paragraph 13, with reference to independent claim 21 and its dependent claims, the Examiner asserts that the first and second magnetic particles could be the same, and therefore interprets the claims as encompassing the use of but one type of magnetic particle to perform all functions. Applicants acknowledge that first and second magnetic particles could be the same, as pointed out at page 14, lines 9-11 of the specification.

Further, the Examiner interprets the claims as encompassing one *specific nucleic acid sequence* present in a broadly heterogenous mixture of nucleic acids. The Examiner's point is well-taken. Applicants did not intend to convey that one could isolate a particular *sequence* from a complex mixture of nucleic acids. In fact, Applicants intended to convey that using the methods of the invention, one could isolate a broader class of nucleic acid molecules (e.g., plasmid DNA, total RNA, mRNA, or genomic DNA) from a mixture of classes of nucleic acids (e.g., see page 6, lines 13-16 or page 8, lines 28-30). The claims as presently amended make this distinction.

At paragraph 14 of the Office Action, the Examiner asserts that Example 7 is the most relevant to the methods, and that it does not disclose the cell type, but inferred that the cell

was bacterial. In fact, the cell type is disclosed as being [*E. coli*] DH5α (page 24, line 9). The Examiner also acknowledges Applicants' Examples teach isolating target nucleic acid from human blood or mouse tissue. Applicants respectfully submit that the claims as amended are fully enabled by Applicants' disclosure. Although Applicants have not exemplified every cell type, they have provided Examples using at least three different sources of starting material. As one of skill in the art would appreciate, under a given set of conditions, the interaction between a target nucleic acid material and a particle will generally be the same, regardless of the source of the target nucleic acid.

Claims 8-20

Although claims 8-20 were rejected under 35 U.S.C. 112, first paragraph as not being enabled by the specification, Applicants were unable to discern where in the Office Action the basis for the rejection was provided. Applicants respectfully request clarification with regard to this rejection.

Rejections under 35 U.S.C. 112, second paragraph

Claims 1-6, 8-14, 21-25, and 27-29 were rejected under 35 U.S.C. 112, second paragraph as being indefinite.

Claims 1-6, 8-14, 21-25, and 27-29 were rejected for reciting that the cells bind directly to the particles, rather than to the hydrous siliceous oxide adsorptive surface. According to the Examiner's suggestion, Applicants have deleted the term "directly," thereby obviating the rejection.

Claims 1-6, 8-14, 21-25, and 27-29 were said to be indefinite with respect to whether pH dependent ion exchange particles, silica magnetic particles or both "consists essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface." The particles to which the Examiner refers form a Markush group, which was introduced by Examiner's amendment mailed with a Notice of Allowance on September 5, 2000. The Markush group is reproduced below:

> "wherein said magnetic particles are selected from the group consisting of (1) pH dependent ion exchange particles and (2) silica magnetic particles consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface..."

Applicants believe that the two types of particles are clearly separated by numerals (1) and (2), and that the "consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface..." is intended to refer only to the silica

magnetic particles. This construction is supported by the fact that the pH dependent ion exchange particles, even pH dependent ion exchange particles comprising a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface, would be modified such that the essential character would be changed.

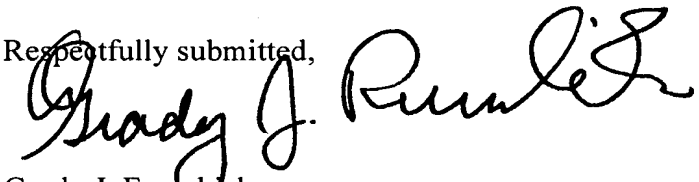
Claim 8 is said to be confusing because line 4 refers to "second magnetic particle" without reference to a first magnetic particle. With due respect, Applicants amended claim 8 by amendment submitted November 5, 2001 to delete the reference to second magnetic particle. In follow up to our supplemental submission of June 25, 2003, Applicants again request acknowledgement that the amendment submitted November 5, 2001 was entered.

Claim 21 is rejected as being indefinite for the recitation of "first magnetic particles" at lines 5-6 because "first magnetic particles" lacks an antecedent basis. The Examiner suggested replacing "first magnetic particles" with "the first magnetic particles." With due respect, to add the definite article "the" before the first occurrence of "first magnetic particles" would render the term indefinite.

As the application is now in condition for allowance, Applicants respectfully request withdrawal of all rejections and allowance of the claims.

This response is accompanied by Check No. 50239 in the amount of $420.00 to cover the fee required under 37 C.F.R. 1.17(a)(2). No other fee is believed due in connection with this submission. If another fee is owing, please charge such fee to deposit account number 50-042.

Respectfully submitted,



Grady J. Frenchick
Reg. No.

Docket No.: 016026-9038
Michael Best & Friedrich LLP
One South Pinckney Street
P. O. Box 1806
Madison, WI 53701-1806
(608) 257-3501